## REMARKS

The present amendment was made to clarify the invention. Claims 421 and 422 were cancelled and new claims 433-444 were added. Support for new claims 433-444 can be found in the application as originally filed. See the specification, for instance, at page 77 (whole page) to page 79, line 10. Claims 407-420, 423, 424, and 433-444 are pending in this case. No new matter has been added to the application as a result of the present amendment.

Prompt consideration and entry of this amendment prior to examination is respectfully requested. The Commissioner is authorized to deduct any fees associated with this amendment from Deposit Account No. 13-2490.

Respectfully submitted,

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## APPENDIX

(clean copy of claims after amendment)

407. A method of detecting a nucleic acid having at least two portions comprising:

(a) contacting the nucleic acid with a substrate having oligonucleotides attached thereto, the oligonucleotides being located between a pair of electrodes, the oligonucleotides having a sequence complementary to a first portion of the sequence of said nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the substrate with said nucleic acid;

(b) contacting said nucleic acid bound to the substrate with a first type of nanoparticles, the nanoparticles being made of a material which can conduct electricity, the nanoparticles having one or more types of oligonucleotides attached thereto, at least one of the types of oligonucleotides having a sequence complementary to a second portion of the sequence of said nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles with said nucleic acid; and

(c) detecting a change in conductivity.

408. The method of Claim 407 wherein the substrate has a plurality of pairs of electrodes located on it in an array to allow for the detection of multiple portions of a single nucleic acid, the detection of multiple different nucleic acids, or both, each of the pairs of electrodes having a type of oligonucleotides attached to the substrate between them.

409. The method of Claim 407 wherein the nanoparticles are made of metal.

410. The method of Claim 407 wherein the nanoparticles are made of gold or silver.

411. The method of Claim 407 wherein the substrate is contacted with silver stain to produce the change in conductivity.

412. The method of Claim 407 further comprising:

(d) contacting the first type of nanoparticles bound to the substrate with a second type of nanoparticles, the nanoparticles being made of a material which can conduct electricity,

the nanoparticles having oligonucleotides attached thereto, at least one of the types of oligonucleotides on the second type of nanoparticles comprising a sequence complementary to the sequence of one of the types of oligonucleotides on the first type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the first and second types of nanoparticles; and

(e) detecting the change in conductivity.

413. The method of Claim 412 wherein at least one of the types of oligonucleotides on the first type of nanoparticles has a sequence complementary to the sequence of at least one of the types of oligonucleotides on the second type of nanoparticles and the method further comprises:

(f) contacting the second type of nanoparticles bound to the substrate with the first type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the first and second types of nanoparticles; and

(g) detecting the change in conductivity.

414. The method of Claim 413 wherein step (d) or steps (d) and (f) are repeated one or more times and the change in conductivity is detected.

415 The method of Claim 407 further comprising:

(d) contacting the first type of nanoparticles bound to the substrate with an aggregate probe having oligonucleotides attached thereto, the nanoparticles of the aggregate probe being made of a material which can conduct electricity, at least one of the types of oligonucleotides on the aggregate probe comprising a sequence complementary to the sequence of one of the types of oligonucleotides on the first type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the aggregate probe with the oligonucleotides on the first type of nanoparticles;

(e) and detecting the change in conductivity.

416. A method of detecting nucleic acid having at least two portions comprising:

(a) contacting a nucleic acid with a substrate having oligonucleotides attached thereto, the oligonucleotides being located between a pair of electrodes, the oligonucleotides having a sequence complementary to a first portion of the sequence of said nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the substrate with said nucleic acid;

(b) contacting said nucleic acid bound to the substrate with an aggregate probe comprising nanoparticles having oligonucleotides attached thereto, at least one of the types of oligonucleotides on the aggregate probe comprising a sequence complementary to the sequence of a second portion of said nucleic acid, the nanoparticles of the aggregate probe being made of a material which can conduct electricity, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the aggregate probe with the nucleic acid; and

(c) detecting a change in conductivity.

417. A method of detecting a nucleic acid wherein the method is performed on a substrate, the method comprising detecting the presence, quantity, or both, of the nucleic acid with an optical scanner.

418. The method of Claim 417 wherein the device is a flatbed scanner.

419. The method of Claim 417 wherein the scanner is linked to a computer loaded with software capable of calculating greyscale measurements, and the greyscale measurements are calculated. to provide a quantitative measure of the amount of nucleic acid detected.

420. The method of Claim 417 wherein the scanner is linked to a computer loaded with software capable of providing an image of the substrate, and a qualitative determination of the presence of the nucleic acid, the quantity of the nucleic acid, or both, is made.

423. A kit comprising a substrate having attached thereto at least one pair of electrodes with oligonucleotides attached to the substrate between the electrodes.

424. The kit of Claim 423 wherein the substrate has a plurality of pairs of electrodes attached to it in an array, to allow for the detection of multiple portions of a single nucleic acid, the detection of multiple different nucleic acids, or both.

433. The method according to any one of claims 407, 412, or 416, wherein the oligonucleotides are attached to the nanoparticles in a stepwise ageing process comprising (i) contacting the oligonucleotides with the nanoparticles in a first aqueous solution for a period of time sufficient to allow some of the oligonucleotides to bind to the nanoparticles; (ii) adding at least one salt to the aqueous solution to create a second aqueous solution; and (iii) contacting the oligonucleotides and nanoparticles in the second aqueous solution for an additional period of time to enable additional oligonucleotides to bind to the nanoparticles.

434. The method according to claim 433, wherein the salt solution has an ionic strength sufficient to overcome at least partially the electrostatic attraction or repulsion of the oligonucleotides for the nanoparticles and the electrostatic repulsion of the oligonucleotides for each other.

435. The method of Claim 433 wherein the nanoparticles are metal nanoparticles or semiconductor nanoparticles.

436. The method of Claim 435 wherein the nanoparticles are gold nanoparticles.

437. The method of Claim 436 wherein the oligonucleotides include a moiety comprising a functional group which can bind to a nanoparticle.

438. The method of Claim 433 wherein all of the salt is added to the water in a single addition.

439. The method of Claim 433 wherein the salt is added gradually over time.

440. The method of Claim 433 wherein the salt is selected from the group consisting of sodium chloride, magnesium chloride, potassium chloride, ammonium chloride, sodium acetate, ammonium acetate, a combination of two or more of these salts, one of these salts in a phosphate buffer, and a combination of two or more these salts in a phosphate buffer.

441. The method of Claim 440 wherein the salt is sodium chloride in a phosphate buffer.

442. The method of any one of Claims 407, 412, or 416 wherein the oligonucleotides present on surface of the nanoparticles at a surface density of at least 10 picomoles/$cm^2$.

443. The method of Claim 442 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of at least 15 picomoles/$cm^2$.

444. The method of Claim 443 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of from about 15 picomoles/$cm^2$ to about 40 picomoles/$cm^2$.